



General

Guideline Title

Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation.

Bibliographic Source(s)

Lucey MR, Terrault N, Ojo L, Hay JE, Neuberger J, Blumberg E, Teperman LW. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Liver Transpl. 2013 Jan;19(1):3-26. [115 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [April 8, 2016 – Metformin-containing Drugs](#) : The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function.

Recommendations

Major Recommendations

The grading system for the strength of recommendations (1 or 2) and the levels of evidence (A–C) is defined at the end of the "Major Recommendations" field.

[Liver Tests](#)

1. The frequency of monitoring with liver tests should be individualized by the transplant center according to the time from liver transplantation (LT), the complications from LT, the stability of serial test results, and the underlying cause (Grade 1, Level A).
2. Depending on the pattern of liver tests, magnetic resonance imaging, computed tomography, endoscopic retrograde cholangiopancreatography, and sonography may be appropriate (Grade 1, Level A).
3. Liver histology should be obtained when parenchymal injury is suspected as the cause of abnormal liver tests (Grade 1, Level A).

Vascular Thrombosis

4. Bilomas and biliary cast syndrome should be managed in a center with expertise in LT medicine, radiology, and biliary endoscopy (Grade 1, Level A).
5. Hepatic artery thrombosis or stenosis is most readily assessed initially by Doppler ultrasound, but angiography is usually required to confirm the diagnosis and plan therapy (Grade 1, Level B).

Late Rejection

6. Immunosuppressive drugs for LT recipients should be prescribed and monitored only by those with knowledge and expertise in that area. The choice of agents will depend on many factors, and no one regimen can be recommended for any patient (Grade 2, Level A).
7. Every patient's immunosuppressive regimen should be reviewed at least every 6 months and modified as required with the goal of minimizing long-term toxicities (Grade 1, Level B).
8. Rejection can be reliably diagnosed only on the basis of liver histology; a biopsy sample should be taken before treatment initiation and classified according to the Banff criteria (Grade 1, Level A).
9. Although the long-term withdrawal of all immunosuppression can be achieved in a small number of patients, this should be undertaken only with select recipients and under close supervision (Grade 2, Level C).

Promoting Health After LT

10. Frequent handwashing reduces the risk of infection with pathogens acquired by direct contact, including *Clostridium difficile*, community-acquired viral infections, and pathogens found in soil (Grade 1, Level A).
11. Shoes, socks, long-sleeve shirts, and long pants should be worn for activities that will involve soil exposure and tick exposure and also to avoid unnecessary sun exposure (Grade 1, Level A).
12. During periods of maximal immunosuppression, LT recipients should avoid crowds to minimize exposures to respiratory illnesses (Grade 1, Level A).
13. Work in high-risk areas, such as construction, animal care settings, gardening, landscaping, and farming, should be reviewed with the transplant team to develop appropriate strategies for the prevention of high-risk exposures (Grade 2, Level A).
14. LT recipients should avoid the consumption of water from lakes and rivers (Grade 1, Level A).
15. LT recipients should avoid unpasteurized milk products and raw and undercooked eggs and meats (particularly uncooked pork, poultry, fish, and seafood; Grade 1, Level A).
16. LT recipients should avoid high-risk pets, which include rodents, reptiles, chicks, ducklings, and birds (Grade 1, Level A).
17. Travel by LT recipients, especially to developing countries, should be reviewed with the transplant team a minimum of 2 months before departure to determine optimal strategies for the reduction of travel-related risks (Grade 1, Level A).
18. LT recipients should take precautions to prevent vector (including mosquito)-borne diseases. These include avoiding going out during peak mosquito feeding times (dawn and dusk) and using *N,N*-diethyl-*meta*-toluamide-containing insect repellants (Grade 1, level A).
19. LT recipients should undertake a thorough review of hobbies to assess potential infectious disease risks, particularly those associated with outdoor hobbies (Grade 2, Level A).
20. All LT recipients should be educated about the importance of sun avoidance and sun protection through the use of a sun block with a sun protection factor of at least 15 and protective clothing. They should be encouraged to examine their skin on a regular basis and report any suspicious or concerning lesions to their physicians (Grade 1, Level A).
21. Because of the strong association of lung, head, and neck cancers with smoking, the sustained cessation of smoking is the most important preventative intervention (Grade 1, Level A).
22. For female LT recipients of a child-bearing age, preconception counseling about contraception and the risks and outcomes of pregnancy should start in the pretransplant period and should be reinforced after transplantation (Grade 1, Level A).

Bone Health

23. In the first 5 years after transplantation, screening by bone mineral density (BMD) should be done yearly for osteopenic patients and every 2 to 3 years for patients with normal BMD; thereafter, screening depends on the progression of BMD and on risk factors (Grade 2, Level B).
24. If osteopenic bone disease is confirmed or if atraumatic fractures are present, then patients should be assessed for risk factors for bone loss;

- in particular, this should include an assessment of calcium intake and 25-hydroxyvitamin D levels, an evaluation of gonadal and thyroid function, a full medication history, and thoracolumbar radiography (Grade 1, Level A).
25. The osteopenic LT recipient should perform regular weight-bearing exercise and receive calcium and vitamin D supplements (Grade 1, Level A).
 26. Bisphosphonate therapy should be considered in LT recipients with osteoporosis or recent fractures (Grade 1, Level A).

Systemic Disease

Kidney Disease

27. Monitoring of renal function in LT recipients for the detection and management of chronic kidney disease (CKD) should use an estimating equation to evaluate the glomerular filtration rate (Grade 1, Level B).
28. Urinary protein quantification using the concentration ratio of protein to creatinine in a spot urine specimen should be evaluated at least once yearly (Grade 1, Level B).
29. The reduction or withdrawal of calcineurin inhibitors (CNI)-associated immunosuppression is an appropriate response to the development of CKD in LT recipients (Grade 1, Level A).
30. Kidney transplantation from deceased or living donors is beneficial in improving survival and should be considered the optimal therapy for LT recipients who develop end-stage renal disease (ESRD) (Grade 1, Level A).

Diabetes Mellitus (DM)

31. The treatment of DM after LT should aim for a hemoglobin A1c (HBA1c) target goal of <7.0% with a combination of lifestyle modifications and pharmacological agents as appropriate (Grade 1, Level B).
32. When high-dose corticosteroids are administered, insulin therapy is the most effective and safest agent with which to control hyperglycemia; however, as the interval from LT extends, patients with new-onset diabetes mellitus (NODM) may experience a decline in insulin requirements, and oral hypoglycemic agents may be appropriate if allograft function is normal (Grade 1, Level C).
33. Metformin or sulfonylureas may be used in LT recipients with normal renal function, whereas sulfonylureas such as glipizide and glimepiride are preferable if there is any deterioration of renal function (Grade 1, Level C).
34. Consideration can be given to the conversion of immunosuppression from tacrolimus to cyclosporine in LT recipients with poor glycemic control (Grade 2, Level B).

Hypertension

35. The treatment of hypertension should aim for a target goal of 130/80 mm Hg with a combination of lifestyle modifications and pharmacological agents as appropriate (Grade 1, Level A).
36. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and direct renin inhibitors should be used as first-line antihypertensive therapy in LT recipients with DM, CKD, and/or significant proteinuria (Grade 1, Level A).

Hyperlipidemia

37. The measurement of blood lipids after a 14-hour fast is recommended annually for healthy LT recipients. An elevated low-density lipoprotein cholesterol level >100 mg/dL, with or without hypertriglyceridemia, requires therapy. If therapeutic lifestyle and dietary changes are not enough, statin therapy should be introduced. Suboptimal control with statins can be improved by the addition of ezetimibe (Grade 2, Level B).
38. Isolated hypertriglyceridemia is first treated with omega-3 fatty acids (up to 4 g daily if tolerated). If this is not sufficient for control, gemfibrozil or fenofibrate can be added, although patients must be followed carefully for side effects, especially with the concomitant use of statins and CNIs (Grade 2, Level C).

Nutrition and Obesity (Body Mass Index >30 kg/m²)

39. All LT patients require ongoing dietary counseling to avoid obesity (Grade 1, Level C).
40. Among LT recipients who become severely or morbidly obese and fail behavioral weight-loss programs, bariatric surgery may be considered, although the optimal procedure and its timing with respect to transplantation remain to be defined (Grade 1, Level C).

Oncology

Recurrent or Persistent Cancer

41. All LT recipients should see a dermatologist after transplantation to assess cutaneous lesions, with at least an annual evaluation by a

- dermatologist 5 years or more after transplantation (Grade 1, Level A).
42. Patients with primary sclerosing cholangitis (PSC) and inflammatory bowel disease or other established risk factors for colorectal cancer should undergo an annual screening colonoscopy with biopsies. Colectomy, including continence-preserving pouch operations, should be considered when colonic biopsy reveals dysplasia (Grade 1, Level B).
 43. For patients without prior hepatocellular carcinoma (HCC) who develop recurrent cirrhosis of the allograft, surveillance for de novo HCC should be undertaken with abdominal imaging every 6 to 12 months (Grade 1, Level A).
 44. An immunosuppressant regimen that includes sirolimus (started several weeks after transplantation) should be considered for patients undergoing transplantation for HCC (Grade 2, Level B).
 45. Resection or ablation is usually the treatment of choice for a solitary extrahepatic metastasis or an intrahepatic recurrence of HCC (Grade 1, Level B).

Reproductive Health

46. Pregnancy in an LT recipient should be managed by a high-risk obstetrician in coordination with the transplant hepatologist (Grade 1, Level C).
47. Pregnancy should be delayed for 1 year after LT and occur at a time with good, stable allograft function, with maintenance immunosuppression, and with good control of any medical complications such as hypertension and diabetes (Grade 1, Level B).
48. The ideal immunosuppression for pregnancy is tacrolimus monotherapy, which should be maintained at therapeutic levels throughout pregnancy; cyclosporine, azathioprine, and prednisone may also be used if they are necessary (Grade 1, Level B).
49. Allograft function and CNI serum levels are monitored every 4 weeks until 32 weeks, then every 2 weeks, and then weekly until delivery (Grade 1, Level B).
50. Contraception should begin before the resumption of sexual activity, although no particular form of contraception can be recommended over another (Grade 2, Level B).

Infectious Disease

General Overview

51. An assessment for infections following LT should take into account the intensity of immunosuppression, the timing of the presentation, the environmental and donor exposures, the recipient's history of both symptomatic and latent infections, and the utilization of prophylactic antimicrobials and immunizations (Grade 1, Level A).
52. Attention should be paid to potential drug interactions when new antimicrobial therapies are initiated (Grade 1, Level A).

Cytomegalovirus (CMV)

53. High-risk recipients (CMV-seronegative recipients of CMV-seropositive donor organs) should receive prophylaxis with ganciclovir or valganciclovir for a minimum of 3 months after transplantation (Grade 1, Level B).
54. The treatment of LT recipients with CMV should be maintained until viremia and all symptoms have resolved (Grade 2, Level B).
55. Prophylaxis against CMV should be resumed whenever LT recipients receive anti-lymphocyte therapy for the treatment of rejection and should be continued for 1 to 3 months after the treatment of rejection (Grade 2, Level B).
56. The treatment of a CMV infection should consist of the following:
 - a. Consideration of immunosuppression reduction.
 - b. High-dose intravenous ganciclovir or oral valganciclovir in individuals with mild to moderate disease without gastrointestinal involvement or a reduced capacity for absorption.
 - c. A minimum of 2 weeks of treatment. Treatment should be continued to complete the resolution of all symptoms and viremia (Grade 1, Level A).
57. Resistant virus should be suspected in patients with a history of prolonged ganciclovir or valganciclovir exposure who have a persistent or progressive infection despite treatment with high-dose intravenous ganciclovir (Grade 1, Level A). In such instances, genotypic assays should be performed, and consideration should be given to the initiation of foscarnet with or in substitution for ganciclovir (Grade 1, Level B).

Epstein-Barr Virus (EBV)/ Posttransplant Lymphoproliferative Disorder (PTLD)

58. PTLD should be considered in LT recipients (especially high-risk individuals) who present with unexplained fever, lymphadenopathy, or cytopenias (Grade 1, Level A).
59. Although EBV may be associated with the development of PTLD, the detection of EBV viremia is not diagnostic for PTLD; a histopathological diagnosis is required (Grade 1, Level A).

Fungal Infections

60. The diagnosis of fungal infections may require diagnostic biopsy for pathological and microbiological confirmation (Grade 1, Level A).
 - a. Blood cultures are most helpful for the diagnosis of *Candida* bloodstream infection (Grade 1, Level B) and *Blastomyces* (Grade 1, Level B).
 - b. Cryptococcal antigen testing of cerebrospinal fluid or blood is most helpful for the diagnosis of *Cryptococcus* (Grade 1, Level B).
 - c. Urinary histoplasmosis and *Blastomyces* antigens are useful for the diagnosis of disseminated histoplasmosis and blastomycosis, respectively (Grade 1, Level B).
61. A cautious reduction of immunosuppression should be initiated to prevent immune reconstitution syndrome, especially for cryptococcal infections (Grade 1, Level B).

Pneumocystis jirovecii (*Pneumocystis carinii*)

62. All LT recipients should receive prophylaxis against *P. jirovecii* with trimethoprim-sulphamethoxazole (single strength daily or double strength 3 times per week) for a minimum of 6 to 12 months after transplantation (Grade 1, Level A). Atovaquone and dapsone are the preferred alternatives for patients who are intolerant of trimethoprim-sulphamethoxazole (Grade 1, Level B).
63. Trimethoprim-sulphamethoxazole is the drug of choice for the treatment of *P. jirovecii* pneumonia. Intravenous pentamidine is the preferred alternative for patients intolerant of trimethoprim-sulphamethoxazole with more severe infections (Grade 1, Level A).
64. Patients with clinical signs and symptoms or radiological features suggestive of *P. jirovecii* pneumonia should undergo sputum sampling or bronchoalveolar lavage with a cytological examination using a silver or Giemsa stain, polymerase chain reaction, or a specific antibody stain to identify the organism (Grade 1, Level A).

Tuberculosis (TB)

65. The treatment of active TB should include the initiation of a 4-drug regimen using isoniazid, rifampin, pyrazinamide, and ethambutol (under the assumption of susceptible TB) with adjustments in accordance with subsequent culture results. This may be tapered to 2 drugs (isoniazid and rifampin) after 2 months (under the assumption of no resistance) and continued for a minimum of 4 additional months (Grade 1, Level B).
66. Close monitoring for rejection and hepatotoxicity is imperative while LT recipients receive anti-TB therapy (Grade 1, Level A).

Human Immunodeficiency Virus (HIV)

67. HIV-infected LT recipients receiving highly active antiretroviral therapy (HAART) require frequent monitoring of CNI levels because of the significant interaction between antiretrovirals and CNIs (Grade 1, Level A).
68. HIV-infected LT recipients receiving HAART should be followed with scheduled HIV viral loads and T lymphocyte subset counts (Grade 1, Level A).
69. Standard prophylaxis for CMV is recommended for HIV-infected LT recipients receiving HAART, and lifelong *Pneumocystis* pneumonia prophylaxis is the norm (Grade 1, Level A).
70. Standard HIV-specific prophylaxis for low cluster of differentiation 4 (CD4) counts should be used (Grade 1, Level A).

Immunizations

71. All LT recipients should receive an annual influenza vaccination (Grade 1, Level B).
72. All LT recipients should avoid live virus vaccines (Grade 1, Level A).
73. Re-immunization is indicated for some vaccines, notably the influenza vaccine (annually) and the pneumococcal vaccine (every 3-5 years; no class or level provided). (Grade 1, Level A).

Viral Hepatitis

Hepatitis B Virus (HBV)

74. Long-term prophylactic therapy using a combination of antiviral agents and low-dose hepatitis B immune globulin (HBIG) on demand or at fixed intervals can effectively prevent HBV recurrence rates in $\geq 90\%$ of transplant recipients (Grade 1, Level B).
75. In patients with low or undetectable HBV deoxyribonucleic acid (DNA) levels before transplantation and an absence of high-risk factors for recurrence, HBIG can be discontinued, and long-term treatment with antivirals (single or in combination) can be used as an alternative prophylactic strategy (Grade 2, Level B).
76. Lifelong antiviral therapy should be used to treat patients with recurrent HBV infections. Combination antiviral therapy is superior to monotherapy when drugs with a low genetic barrier to resistance are used, whereas the discontinuation of HBIG is generally reserved for

patients at low risk for HBV recurrence (Grade 1, Level B).

77. Retransplantation for recurrent HBV is appropriate when treatment strategies to prevent or treat recurrent HBV disease are available (Grade 1, Level C).

Hepatitis C Virus (HCV)

78. Liver biopsy is useful in monitoring disease severity and progression and in distinguishing recurrent HCV disease from other causes of liver enzyme elevations (Grade 1, Level C).
79. Prophylactic antiviral therapy has no current role in the management of HCV disease (Grade 1, Level A).
80. Moderate acute rejection should be treated with increased maintenance immunosuppression and corticosteroid boluses, whereas lymphocyte-depleting drugs should be avoided (Grade 1, Level B).
81. Antiviral therapy is indicated for significant histological disease: grade 3 or higher inflammatory activity and/or stage 2 or higher fibrosis (on a scale of 4) or cholestatic hepatitis. Peginterferon and ribavirin are the current drugs of choice. The risks and benefits of triple therapy with protease inhibitors are to be determined. The goal of antiviral therapy is the achievement of a sustained virological response, and this confers a survival benefit (Grade 1, Level B).
82. Retransplantation for recurrent HCV disease should be considered selectively (Grade 2, Level B).

Primary Biliary Cirrhosis (PBC)

83. PBC LT recipients should be routinely monitored for associated autoimmune diseases (e.g., thyroid disease) and bone density (Grade 2, Level B).
84. For those with histological evidence of recurrent disease, treatment with ursodeoxycholic acid at 10 to 15 mg/kg/day (Grade 2, Level B) may be considered, and although its use is associated with the improvement of liver tests, no impact on graft survival has been documented (Grade 2, Level B). There is no indication for offering prophylaxis with ursodeoxycholic acid to patients with normal liver histology (Grade 2, Level B).

Primary Sclerosing Cholangitis (PSC)

85. Although there are few data on prevention, it is recommended that those patients grafted for PSC in the presence of chronic ulcerative colitis (CUC) have an annual colonoscopy with mucosal biopsy (Grade 2, Level B).

Autoimmune Hepatitis (AIH)

86. Although there is no evidence for recommending a particular immunosuppressive regimen in patients undergoing transplantation for AIH, it is prudent to maintain patients on long-term, low-dose corticosteroids in addition to routine immunosuppression (with attention to maintaining bone health; Grade 2, Level B).

Alcoholic Liver Disease (ALD)

87. All patients with a prior diagnosis of ALD should be encouraged to remain abstinent from alcohol (Grade 1, Level B).
88. Patients should be encouraged to enter therapy or counseling if they relapse into alcohol use (Grade 1, Level C).
89. All patients with a prior diagnosis of ALD who are users of tobacco should be encouraged to undertake smoking cessation (Grade 1, Level B).
90. Careful attention should be given to the risk of cardiovascular disease and/or new-onset cancers of the aerodigestive tract, especially in cigarette smokers (Grade 1, Level A).

Nonalcoholic Steatohepatitis (NASH)/ Nonalcoholic Fatty Liver Disease (NAFLD)

91. The confirmation of recurrent or de novo NAFLD, the recognition of fibrosis, and the exclusion of alternate causes of elevated liver chemistry tests require liver biopsy (Grade 1, Level B).
92. No specific recommendations regarding the prevention or treatment of NAFLD or NASH in LT recipients can be made other than general recommendations to avoid excessive gains in body weight and control hypertension and diabetes (Grade 1, Level C).

Late Surgical Complications

93. LT recipients with an incisional hernia should be instructed to recognize incarcerated hernias and advised to seek immediate medical assistance (Grade 1, Level B).

Definitions:

Quality of Evidence*

Quality of Evidence	Criteria
A. High	Further research is unlikely to change confidence in the estimate of the clinical effect.
B. Moderate	Further research may change confidence in the estimate of the clinical effect.
C. Low	Further research is very likely to affect confidence in the estimate of the clinical effect.

Strength of Recommendations*

Strength of Recommendation	Criteria
1. Strong	Factors influencing the strength of the recommendation included the quality of the evidence, the presumed patient-important outcomes, and the cost
2. Weak	There is variability in the preferences and values or more uncertainty. The recommendation is made with less certainty, or the cost or resource consumption is higher.

*Classification used by the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) workgroup with minor modifications

Clinical Algorithm(s)

None available

Scope

Disease/Condition(s)

Liver transplantation (LT)

Guideline Category

Diagnosis

Management

Prevention

Treatment

Clinical Specialty

Family Practice

Gastroenterology

Internal Medicine

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide a data-supported approach to management of adult patients who have successfully undergone liver transplantation (LT)
- To suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care of adult patients who have successfully undergone liver transplantation (LT)

Target Population

Adult patients who have successfully undergone liver transplantation (LT)

Interventions and Practices Considered

1. Liver testing
2. Liver magnetic resonance imaging, computed tomography, endoscopic retrograde cholangiopancreatography, and sonography
3. Liver histology
4. Management of bilomas and biliary cast syndrome in a center with expertise in liver transplant medicine, radiology, and biliary endoscopy
5. Doppler ultrasound and angiography to assess hepatic artery thrombosis or stenosis
6. Immunosuppressive agents
 - Monitoring and review
 - Long-term withdrawal
7. Health promotion
 - Frequent hand washing to reduce infection risk
 - Wearing shoes, socks, long-sleeve shirts, and long pants for activities that will involve soil exposure and tick exposure
 - Sun protection and avoidance of unnecessary sun exposure
 - Avoidance crowds to minimize exposures to respiratory illnesses
 - Review and development of appropriate strategies for the prevention of high-risk work exposures in high-risk areas, (e.g., construction, animal care settings, gardening, landscaping, farming)
 - Avoidance of consumption of water from lakes and rivers
 - Avoidance of unpasteurized milk products, raw and undercooked eggs and meats (particularly uncooked pork, poultry, fish and seafood)
 - Avoidance of high-risk pets, including rodents, reptiles, chicks, ducklings, and birds
 - Review and development of strategies for traveling to developing countries
 - Precautions to prevent vector (including mosquito)-borne diseases
 - Review of hobbies to assess potential infectious disease risks, (particularly those associated with outdoor hobbies)
 - Smoking cessation
 - Counseling female patients about contraception and the risks and outcomes of pregnancy

Major Outcomes Considered

- Survival rates
- Incidence and severity of complications

- Incidence of late rejection
- Quality of life
- Symptom control

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A literature search of MEDLINE and PubMed with end date April 2012 was performed; no pre-specified search terms were utilized. The writing group divided the guideline into 21 sections distributed among 7 members of the writing group and each member of the writing group performed the comprehensive literature search for the section they were responsible for writing. Within each subgroup, members were instructed to crosscheck and verify the completeness of the literature search. The Chair of the writing group has independently performed the literature search for all sections to verify that the literature search was comprehensive and was without any obvious bias.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence*

Quality of Evidence	Criteria
A. High	Further research is unlikely to change confidence in the estimate of the clinical effect.
B. Moderate	Further research may change confidence in the estimate of the clinical effect.
C. Low	Further research is very likely to affect confidence in the estimate of the clinical effect.

*Classification used by the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) workgroup with minor modifications

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

These recommendations provide a data-supported approach to management of adult patients who have successfully undergone liver transplantation (LT). The recommendations are based on the following: (1) a formal review and analysis of recently published world literature on the topic; (2) *A Manual for Assessing Health Practices and Designing Practice Guidelines* (American College of Physicians); (3) guideline policies, including the American Association for the Study of Liver Diseases (AASLD) policy on the development and use of practice guidelines and the American Gastroenterological Association (AGA) policy statement on guidelines; and (4) the experience of the authors in the specified topic.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations*

Strength of Recommendation	Criteria
1. Strong	Factors influencing the strength of the recommendation included the quality of the evidence, the presumed patient-important outcomes, and the cost
2. Weak	There is variability in the preferences and values or more uncertainty. The recommendation is made with less certainty, or the cost or resource consumption is higher.

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Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline document was produced in collaboration with the American Association for the Study of Liver Diseases (AASLD) Practice Guidelines Committee, which provided extensive peer review of the manuscript.

This practice guideline was approved by the AASLD on August 4, 2012 and by the American Society of Transplantation on September 19, 2012.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate long-term management of liver transplant patients

Potential Harms

- The continued use of immunosuppression carries inevitable consequences: an increased risk of bacterial, viral, and fungal infections, which can be recurrent or newly acquired; metabolic complications such as hypertension, diabetes mellitus (DM), hyperlipidemia, obesity, and gout; and hepatobiliary or extrahepatic de novo cancers (including posttransplant lymphoproliferative disorder [PTLD]).
- Because of the increased risk of electrolyte abnormalities, thiazide or loop diuretics should be used with caution.
- The use of highly active antiretroviral therapy (HAART) in liver transplantation (LT) recipients is complicated by significant drug-drug interactions with immunosuppressive agents, which lead to a risk of cyclosporine or tacrolimus toxicity or inadequate immunosuppression.

Qualifying Statements

Qualifying Statements

Intended for use by physicians and health care providers working with adult recipients of liver transplantation (LT), these recommendations suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care. They are intended to be flexible, in contrast to standards of care, which are inflexible policies to be followed in every case. Specific recommendations are based on relevant published information.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Lucey MR, Terrault N, Ojo L, Hay JE, Neuberger J, Blumberg E, Teperman LW. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Transpl*. 2013 Jan;19(1):3-26. [115 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Jan

Guideline Developer(s)

American Association for the Study of Liver Diseases - Nonprofit Research Organization

American Society of Transplantation - Professional Association

Source(s) of Funding

American Association for the Study of Liver Diseases (AASLD)

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Guideline Committee

Practice Guidelines Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Potential conflicts of interest: Dr. Teperman is on the speakers' bureau for and received grants from Gilead. He is on the speakers' bureau for Vertex and advises VTF. Dr. Ojo advises Novartis and Sanofi. Dr. Lucey consults for Alkermes and received grants from Vertex, Abbot, and Gilead. Dr. Blumberg received grants from Viropharma and is on the data safety monitoring boards for Pfizer and Chimerix. Dr. Terrault consults for and received grants from Roche, Genentech, and Gilead. She also consults for Bristol Myers Squibb, Bitotest, Merck, and Siemens and received grants from Novartis, Eisai, and Vertex.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [American Association for the Study of Liver Diseases Web site](#)

Print copies: Reprint requests to Michael R. Lucey, M.D., Division of Gastroenterology and Hepatology, Department of Medicine, University of Wisconsin School of Medicine and Public Health, 1685 Highland Avenue, 4245 MFMB, Madison, WI 53792-5124. Telephone: 608-263-7322; Fax: 608-265-5677; E-mail: mrl@medicine.wisc.edu.

Availability of Companion Documents

This guideline is available as a Personal Digital Assistant (PDA) download via the APPRISOR™ Document Viewer from www.apprisor.com

Patient Resources

None available

NGC Status

This summary was completed by ECRI Institute on July 22, 2013. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs.

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